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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,645	06/29/2001	Nicholas Yuri Chirgadze	X-13948	9746

7590 12/24/2003

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EXAMINER	
NASHED, NASHAAT T	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,645	CHIRGADZE ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *15-19 and 21-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-14,20 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election without traverse of Group I, claims 1-14, 20, and 29-31 in the paper filed October 6, 2003 is acknowledged. Thus, claims 15-19, are 21-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected without traverse, there being no allowable generic or linking claim.

Claims 1-14, 20, and 29-31 are pending in this Office action.

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The instant application names four inventor. Only, Nicholas Yuri Chirgadze has signed the declaration of record. An executed declaration signed by Stephen Briggs, Genshi Zhao, and Kelly McAllister is required.

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims 20 and 29-30 are objected to because they are dependent on non-elected claims. For examination purposes, all the embodiment of the parent claims are incorporated in the examined claims.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14, 20, and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-14 and 29-31 are directed to all possible crystals of any *Streptococcus pneumoniae* having any amino acid sequence. The specification, however, only provides a single representative species of these crystal of residues 3-122 of SEQ ID NO: 1 belongs to the orthorhombic space group $P2_12_12_1$ with unit cell dimensions of a = 49.8 Å, b = 59.6 Å, and c = 114.7 Å encompassed by these claims. There is no disclosure or gidance in the specification on how one of ordinary skill in the art would change the crystallization conditions with the changing of the primary structure of the single disclosed polypeptide species to obtain the claimed crystal. Also, the specification fails to describe additional representative species of these crystals which effectively diffract X-ray. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 1-14 and 29-39 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a crystal of a protein consisting of residues 3-122 of SEQ ID NO: 1 belongs to orthorhombic space group $P2_12_12_1$ with unit cell dimensions of a = 49.8 Å, b = 59.6 Å, and c = 114.7 Å. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible crystal and their complexes for any *P. pneumoniae* acyl carrier protein synthase. Claims 5, 10, and 14 are directed to a monoclinic crystals having space group symmetry C2 with unit cell dimensions of native and a complex with 3',5'-ADP crystals: a = 120.2, b = 62.3, c = 51.7, and $\beta = 98.7°$ which the specification does not teach how to make. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any crystal of any *P. pneumoniae* acyl carrier protein synthase having any amino acid sequence. The specification provides guidance and examples in the form of an assay to express the polypeptide of residues 3-122 of SEQ ID NO: 1 and crystallize it under specific crystallization condition described on page 66, second paragraph to obtain the orthorhombic crystal. While molecular biological techniques to make any protein fragment and several crystallization methods for proteins are known in the prior art and the skill of the artisan are developed, knowledge regarding how to obtain any protein crystal, and in particular, suitable crystal for structure determination by X-ray is lacking. Thus, searching for a *P. pneumoniae* acyl carrier protein synthase having any amino acid sequence and crystallization conditions to obtain any crystal, let alone, adequate crystal for structure determination by x-ray diffraction method. The conditions of crystallization is highly dependent on the protein itself and any minor change in the amino acid sequence may require search for new crystallization conditions. It is noted that the specification stated that the monoclinic crystals were obtained under similar crystallization conditions described for the orthorhombic crystal, see page 66, line 20, which raises several questions. Does the described crystallization conditions on page 66 produces a mixtures of the orthorhombic and monoclinic crystals? Does it sometime produce one or the other crystal? Does the monoclinic crystal obtained by some how modifying the condition on page 66? if the modification of the conditions described described for the orthorhombic crystal in the specification is required to obtain the monoclinic crystal, what has been done to obtain the monoclinic crystal. Clearly, the specification does not described a reproducible method to obtain at least the monoclinic crystal by a repeatable method. The amount of experimentation to identify an acyl carrier protein from *P. pneumoniae*, purify the desired protein from its natural source or identify the nucleic acid sequence encoding said synthase and develop a recombinant method to obtain the synthase, identify a crystallization conditions to grow a single crystal suitable for structure determination by X-ray is enormous. Producing a co-crystal of an already crystallizable protein may require searching for new crystallization conditions with no expectation of success. The specification itself highlights the unpredictability in the composition of a crystal as it teaches the surprise formation of 3',5'-ADP from a crystalization composition containing the reactants of the reaction catalyzed by the synthase. While the specification teaches method of obtaining the protein of SEQ ID NO: 1 wherein all methionine residues are substituted with selenomethionine, the specification does not teach the crystalization of SEQ ID NO: 1 itself or the selenomethionine derivative of SEQ ID NO: 1. Selenomethionine of SEQ ID NO: 1 is an independent chemical entity and would be expected to have different physical and chemical properties from those of the wild-type SEQ ID NO: 1. Thus, one of ordinary skill in the art would not expect that selenomethionine of SEQ ID NO: 1 would crystallize under the same conditions in the same space group as that of the wild-type. Since routine experimentation in the art does not include screening genomic or cDNA libraries to identify a gene encoding an acyl carrier protein synthase, or purification

methods to identify said synthase, and protein crystallization conditions where the expectation of obtaining the desired crystal is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the exact protein to be crystallized, an exact crystallization conditions, or a compound which would co-crystallize with said synthase, and produce adequate crystal for structural determination by X-ray. Without such a guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "binding site shown in Figure 9" in claim 3 renders the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The binding site is a three dimensional structure, whereas Figure 9 is a two dimensional representation of said structure, and could not be transformed into a three dimensional representation.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were

made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim 20 is rejected under 35 U.S.C. § 103 as being unpatentable over U. S. patent 6,060,282 (282, Tang *et al.*) in view of the prior art as exemplified by Hendrickson *et al.* (only the abstract is provided: EMBO J. Vol. 9, pages 1665-1672) and the well known methods of drug designs using three dimensional structure of target protein.

The 282 patent teaches a gene encoding *Streptococcus pneumoniae* acyl carrier protein synthase of SEQ ID NO: 2 which is identical to the amino acid sequence of SEQ ID NO: 1 of the instant application, see the abstract and column 4, lines 12-19, and that the protein is a target for drug development, column 1, line 24-31, and column 4 lines 38-46. Also, 282 patent teaches vector and host cell comprising the gene and a recombinant method to make the protein of SEQ ID NO: 2, see examples 1 and 2. The patent, however, does not teach the selenomethionine of SEQ ID NO: 2, i. e., SEQ ID NO: 1 of the instant application.

Hendrickson *et al.* teach methods of making proteins comprising substitution of methionine by selenomethionine, see the abstract. Also, they teach the use of proteins comprising selenomethionin in solving the "phasing problem" which is required to obtain a three dimensional structure from X-ray diffraction data using the method of multi-wavelength anomalous diffraction (MAD) method. Such a method would replace the highly laborious classical method of solving the phasing problem which requires the preparation of several isomorphous crystals comprising heavy metals.

The 282 patent provides one of ordinary skill in the art with motivation to develop antibacterial compound that inhibits the action of the protein of SEQ ID NO: 2. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to make the selenomethionine derivative of the protein of SEQ ID NO: 2 taught in the 282 patent by the method taught by Hendrickson *et al.* to attempt to crystallize the protein and solve its three dimensional structure to be used in drug design method. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is

(703) 305-6586. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner